

ALSUMA- sumatriptan injection, solution
Pfizer Laboratories Div Pfizer Inc

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ALSUMA safely and effectively. See full prescribing information for ALSUMA.

ALSUMA (sumatriptan injection) 6 mg/0.5 mL for subcutaneous use
Initial U.S. Approval: 1992

----- **INDICATIONS AND USAGE** -----

ALSUMA is a serotonin (5-HT_{1B/1D}) receptor agonist (triptan) indicated for:

- Acute treatment of migraine with or without aura in adults (1)
- Acute treatment of cluster headache in adults (1)

Limitations of Use:

- Use only if a clear diagnosis of migraine or cluster headache has been established. (1)
- Not indicated for the prophylactic therapy of migraine. (1)

----- **DOSAGE AND ADMINISTRATION** -----

- For subcutaneous use only. (2.1)
- Single 6 mg dose administered to an injection site with adequate skin and subcutaneous thickness (e.g. lateral thigh or upper arm). (2.1)
- The maximum recommended dose in 24 hours is two doses separated by at least 1 hour. (2.1)

----- **DOSAGE FORMS AND STRENGTHS** -----

Injection: 6-mg sumatriptan in a pre-filled, single-use auto-injector (3)

----- **CONTRAINDICATIONS** -----

- History of coronary artery disease or coronary vasospasm (4)
- Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders (4)
- History of stroke, transient ischemic attack, or hemiplegic or basilar migraine (4)
- Peripheral vascular disease (4)
- Ischemic bowel disease (4)
- Uncontrolled hypertension (4)
- Recent (within 24 hours) use of another 5-HT₁ agonist (e.g., another triptan) or an ergotamine-containing medication (4)
- Current or recent (past 2 weeks) use of monoamine oxidase-A inhibitor (4)
- Hypersensitivity to ALSUMA (angioedema and anaphylaxis seen) (4)
- Severe hepatic impairment (4)

----- **WARNINGS AND PRECAUTIONS** -----

- Myocardial ischemia/infarction and Prinzmetal's angina: Perform cardiac evaluation in patients with multiple cardiovascular risk factors. (5.1)
- Arrhythmias: Discontinue ALSUMA if occurs. (5.2)
- Chest/throat/neck/jaw pain, tightness, pressure, or heaviness: Generally not associated with myocardial ischemia; evaluate for coronary artery disease in patients at high risk. (5.3)
- Cerebral hemorrhage, subarachnoid hemorrhage, and stroke: Discontinue ALSUMA if occurs. (5.4)
- Gastrointestinal ischemia and infarction events, peripheral vasospastic reactions. Discontinue ALSUMA if occurs. (5.5)
- Medication overuse headache: Detoxification may be necessary. (5.6)
- Serotonin syndrome: Discontinue ALSUMA if occurs. (5.7)
- Seizures: Use with caution if patients with epilepsy or a lowered seizure threshold. (5.10)

----- **ADVERSE REACTIONS** -----

Most common adverse reactions (≥ 5% and > placebo) were injection site reactions, tingling, dizziness/vertigo, warm/hot sensation, burning sensation, feeling of heaviness, pressure sensation, flushing, feeling of tightness, and numbness (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----- **USE IN SPECIFIC POPULATIONS** -----

- Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 4/2014

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ALSUMA™ (sumatriptan injection) is indicated in adults for the acute treatment of migraine, with or without aura, and the acute treatment of cluster headache.

Limitations of Use:

- Use only if a clear diagnosis of migraine or cluster headache has been established. If a patient has no response to the first migraine attack treated with ALSUMA, reconsider the diagnosis of migraine before ALSUMA is administered to treat any subsequent attacks.
- ALSUMA is not indicated for the prevention of migraine attacks.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The maximum single recommended dose of ALSUMA is 6 mg injected subcutaneously.

The maximum recommended dose that may be given in 24 hours is two doses of ALSUMA separated by at least 1 hour. Controlled clinical trials have failed to show a clear benefit with the administration of a second 6 mg dose in patients who have failed to respond to a first dose. A second 6 mg dose should only be considered if some response to a first injection was observed.

2.2 Administration Using ALSUMA

ALSUMA is only for subcutaneous use. Intramuscular or intravascular delivery must be avoided. Patients should be directed to use injection sites with an adequate skin and subcutaneous thickness to accommodate the length of the needle.

ALSUMA is for single use only. Visually inspect the medication for particulate matter and discoloration before administration. Do not use if particulates and discolorations are noted. Discard unused portions. *[see Patient Counseling Information (17.8)]*

3 DOSAGE FORMS AND STRENGTHS

ALSUMA contains 6 mg of sumatriptan (as 8.4 mg sumatriptan succinate), which is delivered as a subcutaneous injection in a single dose.

ALSUMA is supplied as a single-use auto-injector pre-filled with sumatriptan succinate drug solution and fully-assembled for use.

4 CONTRAINDICATIONS

ALSUMA is contraindicated in patients with:

- Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or documented silent ischemia) or coronary artery vasospasm, including Prinzmetal's angina *[see Warnings and Precautions (5.1)]*.
- Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders *[see Warnings and Precautions (5.2)]*.
- History of stroke or transient ischemic attack (TIA), or history or current evidence of hemiplegic or

basilar migraine because these patients are at a higher risk of stroke [see *Warnings and Precautions (5.4)*].

- Peripheral vascular disease [see *Warnings and Precautions (5.5)*].
- Ischemic bowel disease. [see *Warnings and Precautions (5.5)*].
- Uncontrolled hypertension [see *Warnings and Precautions (5.8)*].
- Recent (i.e., within 24 hours) use of ergotamine-containing medication, ergot-type medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine₁ (5-HT₁) agonist [see *Drug Interactions (7.1, 7.3)*].
- Concurrent administration of an MAO-A inhibitor or recent (within 2 weeks) use of an MAO-A inhibitor [see *Drug Interactions (7.2) and Clinical Pharmacology (12.3)*].
- Hypersensitivity to ALSUMA (angioedema and anaphylaxis seen) [see *Warnings and Precautions (5.9)*].
- Severe hepatic impairment [see *Clinical Pharmacology (12.3)*].

5 WARNINGS AND PRECAUTIONS

5.1 Myocardial Ischemia, Myocardial Infarction, and Prinzmetal's Angina

ALSUMA is contraindicated in patients with ischemic or vasospastic CAD. There have been rare reports of serious cardiac adverse reactions, including acute myocardial infarction, occurring within a few hours following administration of sumatriptan. Some of these reactions occurred in patients without known CAD. ALSUMA may cause coronary artery vasospasm (Prinzmetal's angina), even in patients without a history of CAD.

Perform a cardiovascular evaluation in triptan-naïve patients who have multiple cardiovascular risk factors (e.g., increased age, diabetes, hypertension, smoking, obesity, strong family history of CAD) prior to receiving ALSUMA. If there is evidence of CAD or coronary artery vasospasm, ALSUMA is contraindicated. For patients with multiple cardiovascular risk factors who have a negative cardiovascular evaluation, consider administering the first dose of ALSUMA in a medically supervised setting and performing an electrocardiogram (ECG) immediately following ALSUMA. For such patients, consider periodic cardiovascular evaluation in intermittent long-term users of ALSUMA.

5.2 Arrhythmias

Life-threatening disturbances of cardiac rhythm, including ventricular tachycardia and ventricular fibrillation leading to death, have been reported within a few hours following the administration of 5-HT₁ agonists. Discontinue ALSUMA if these disturbances occur. ALSUMA is contraindicated in patients with Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders.

5.3 Chest, Throat, Neck and/or Jaw Pain/Tightness/Pressure

Sensations of tightness, pain, pressure, and heaviness in the precordium, throat, neck, and jaw commonly occur after treatment with ALSUMA and are usually non-cardiac in origin. However, perform a cardiac evaluation if these patients are at high cardiac risk. The use of ALSUMA is contraindicated in patients shown to have CAD and those with Prinzmetal's variant angina.

5.4 Cerebrovascular Events

Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT₁ agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the 5-HT₁ agonists having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine when they were not. Also, patients with migraine may be at increased risk of certain cerebrovascular events (e.g., stroke, hemorrhage, TIA). Discontinue ALSUMA if a cerebrovascular event occurs.

Before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms, exclude other potentially serious neurological conditions. ALSUMA is contraindicated in patients with a history of stroke or TIA.

5.5 Other Vasospasm Reactions

ALSUMA may cause non-coronary vasospastic reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction (presenting with abdominal pain and bloody diarrhea), splenic infarction, and Raynaud's syndrome. In patients who experience symptoms or signs suggestive of non-coronary vasospasm reaction following the use of any 5-HT₁ agonist, rule out a vasospastic reaction before receiving additional ALSUMA doses.

Reports of transient and permanent blindness and significant partial vision loss have been reported with the use of 5-HT₁ agonists. Since visual disorders may be part of a migraine attack, a causal relationship between these events and the use of 5-HT₁ agonists have not been clearly established.

5.6 Medication Overuse Headache

Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, or combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in frequency of migraine attacks. Detoxification of patients, including withdrawal of the overused drugs and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary.

5.7 Serotonin Syndrome

Serotonin syndrome may occur with ALSUMA, particularly during co-administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors [see *Drug Interactions (7.4)*]. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The onset of symptoms usually occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication. Discontinue ALSUMA if serotonin syndrome is suspected.

5.8 Increase in Blood Pressure

Significant elevation in blood pressure, including hypertensive crisis with acute impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT₁ agonists, including patients without a history of hypertension. Monitor blood pressure in patients treated with ALSUMA. ALSUMA is contraindicated in patients with uncontrolled hypertension.

5.9 Anaphylactic/Anaphylactoid Reactions

There have been reports of anaphylactic, anaphylactoid, and hypersensitivity reactions including angioedema in patients receiving ALSUMA. Such reactions can be life threatening or fatal. In general, anaphylactic reactions to drugs are more likely to occur in individuals with a history of sensitivity to multiple allergens. ALSUMA is contraindicated in patients with a history of hypersensitivity reaction to ALSUMA.

5.10 Seizures

Seizures have been reported following administration of ALSUMA. Some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures. There are also reports in patients where no such predisposing factors are apparent. ALSUMA should be used with caution in patients with a history of epilepsy or conditions associated with a lowered seizure threshold.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the prescribing information:

- Myocardial ischemia, myocardial infarction, and Prinzmetal's angina [see *Warnings and Precautions (5.1)*]
- Arrhythmias [see *Warnings and Precautions (5.2)*]
- Chest, throat, neck, and/or jaw pain/tightness/pressure [see *Warnings and Precautions (5.3)*]
- Cerebrovascular events [see *Warnings and Precautions (5.4)*]
- Other vasospasm reactions [see *Warnings and Precautions (5.5)*]
- Medication overuse headache [see *Warnings and Precautions (5.6)*]
- Serotonin syndrome [see *Warnings and Precautions (5.7)*]
- Increase in blood pressure [see *Warnings and Precautions (5.8)*]
- Hypersensitivity reactions [see *Warnings and Precautions (5.9)*]
- Seizures [see *Warnings and Precautions (5.10)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Migraine Headache:

Table 1 lists adverse reactions that occurred in 2 US placebo-controlled clinical trials in migraine subjects [Studies 2 and 3, see *Clinical Studies (14.1)*] following either a single 6-mg dose of sumatriptan injection or placebo. Only reactions that occurred at a frequency of 2% or more in groups treated with sumatriptan injection 6 mg and that occurred at a frequency greater than the placebo group are included in Table 1.

Table 1. Adverse Reactions Reported by at Least 2% of Subjects and at a Greater Frequency Than Placebo in 2 Placebo-Controlled Migraine Clinical Trials (Studies 2 and 3)*

| Adverse Reaction | Percent of Subjects Reporting | |
|-----------------------|---|-------------------|
| | Sumatriptan 6 mg Subcutaneous (n = 547) | Placebo (n = 370) |
| Atypical sensations | 42 | 9 |
| Tingling | 14 | 3 |
| Warm/hot sensation | 11 | 4 |
| Burning sensation | 7 | <1 |
| Feeling of heaviness | 7 | 1 |
| Pressure sensation | 7 | 2 |
| Feeling of tightness | 5 | <1 |
| Numbness | 5 | 2 |
| Feeling strange | 2 | <1 |
| Tight feeling in head | 2 | <1 |
| Cardiovascular | | |
| Flushing | 7 | 2 |
| Chest Discomfort | 5 | 1 |
| Tightness in chest | 3 | <1 |

| | | |
|----------------------------------|----|----|
| Pressure in chest | 2 | <1 |
| Ear, nose and throat | | |
| Throat discomfort | 3 | <1 |
| Discomfort: nasal cavity/sinuses | 2 | <1 |
| Injection site reaction† | 59 | 24 |
| Miscellaneous | | |
| Jaw discomfort | 2 | 0 |
| Musculoskeletal | | |
| Weakness | 5 | <1 |
| Neck pain/stiffness | 5 | <1 |
| Myalgia | 2 | <1 |
| Neurological | | |
| Dizziness/vertigo | 12 | 4 |
| Drowsiness/sedation | 3 | 2 |
| Headache | 2 | <1 |
| Skin | | |
| Sweating | 2 | 1 |

* The sum of the percentages cited is greater than 100% because subjects may have experienced more than 1 type of adverse reaction. Only reactions that occurred at a frequency of 2% or more in groups treated with sumatriptan injection and occurred at a frequency greater than the placebo groups are included.

† Includes injection site pain, stinging/burning, swelling, erythema, bruising, bleeding.

The incidence of adverse reactions in controlled clinical trials was not affected by gender or age of the subjects. There were insufficient data to assess the impact of race on the incidence of adverse reactions.

Cluster Headache:

In the controlled clinical trials assessing the efficacy of sumatriptan injection as a treatment for cluster headache [Studies 4 and 5, see *Clinical Studies (14.2)*], no new significant adverse reactions were detected that had not already been identified in trials of sumatriptan in subjects with migraine.

Overall, the frequency of adverse reactions reported in the trials of cluster headache was generally lower than in the migraine trials. Exceptions include reports of paresthesia (5% sumatriptan, 0% placebo), nausea and vomiting (4% sumatriptan, 0% placebo), and bronchospasm (1% sumatriptan, 0% placebo).

Adverse Reactions Observed In Association With The Administration of ALSUMA:

The safety of ALSUMA was evaluated in an open-label clinical trial evaluating the usability of ALSUMA during a migraine attack. Adverse reactions that occurred at a frequency of 5% or higher were injection site bruising (16%), injection site pain (6%), and injection site hemorrhage (6%).

7 DRUG INTERACTIONS

7.1 Ergot-Containing Drugs

Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine or methysergide) and ALSUMA within 24 hours of each other is contraindicated.

7.2 Monoamine Oxidase-A Inhibitors

MAO-A inhibitors increase systemic exposure by 2-fold. Therefore, the use of ALSUMA in patients receiving MAO-A inhibitors is contraindicated [see *Clinical Pharmacology (12.3)*].

7.3 Other 5-HT₁ Agonists

Because their vasospastic effects may be additive, co-administration of ALSUMA and other 5-HT₁ agonists (e.g., triptans) within 24 hours of each other is contraindicated.

7.4 Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome

Cases of serotonin syndrome have been reported during co-administration of triptans and SSRIs, or SNRIs, SNRIs, TCAs, and MAO inhibitors [see *Warnings and Precautions (5.7)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. There are no adequate and well-controlled trials of sumatriptan injection in pregnant women. In developmental toxicity studies in rats and rabbits, oral administration of sumatriptan to pregnant animals was associated with embryoletality, fetal abnormalities, and pup mortality. When administered by the intravenous route to pregnant rabbits, sumatriptan was embryoethal. ALSUMA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Oral administration of sumatriptan to pregnant rats during the period of organogenesis resulted in an increased incidence of fetal blood vessel (cervicothoracic and umbilical) abnormalities. The highest no-effect dose for embryofetal developmental toxicity in rats was 60 mg/kg/day. Oral administration of sumatriptan to pregnant rabbits during the period of organogenesis resulted in increased incidences of embryoletality and fetal cervicothoracic vascular and skeletal abnormalities. Intravenous administration of sumatriptan to pregnant rabbits during the period of organogenesis resulted in an increased incidence of embryoletality. The highest oral and intravenous no-effect doses for developmental toxicity in rabbits were 15 and 0.75 mg/kg/day, respectively.

Oral administration of sumatriptan to rats prior to and throughout gestation resulted in embryofetal toxicity (decreased body weight, decreased ossification, increased incidence of skeletal abnormalities). The highest no-effect dose was 50 mg/kg/day. In offspring of pregnant rats treated orally with sumatriptan during organogenesis, there was a decrease in pup survival. The highest no-effect dose for this effect was 60 mg/kg/day. Oral treatment of pregnant rats with sumatriptan during the latter part of gestation and throughout lactation resulted in a decrease in pup survival. The highest no-effect dose for this effect was 100 mg/kg/day.

8.3 Nursing Mothers

Sumatriptan is excreted in human milk following subcutaneous administration. Infant exposure to sumatriptan can be minimized by avoiding breastfeeding for 12 hours after treatment with ALSUMA.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established. ALSUMA is not recommended for use in patients younger than 18 years of age.

Two controlled clinical trials evaluated sumatriptan nasal spray (5 to 20 mg) in 1,248 adolescent migraineurs aged 12 to 17 years who treated a single attack. The trials did not establish the efficacy of sumatriptan nasal spray compared with placebo in the treatment of migraine in adolescents. Adverse reactions observed in these clinical trials were similar in nature to those reported in clinical trials in adults.

Five controlled clinical trials (2 single-attack trials, 3 multiple-attack trials) evaluating oral sumatriptan (25 to 100 mg) in pediatric subjects aged 12 to 17 years enrolled a total of 701 adolescent migraineurs. These trials did not establish the efficacy of oral sumatriptan compared with placebo in the treatment of migraine in adolescents. Adverse reactions observed in these clinical trials were similar in nature to those reported in clinical trials in adults. The frequency of all adverse reactions in these subjects appeared to be both dose- and age-dependent, with younger subjects reporting reactions more commonly than older adolescents.

Postmarketing experience documents that serious adverse reactions have occurred in the pediatric population after use of subcutaneous, oral, and/or intranasal sumatriptan. These reports include reactions similar in nature to those reported rarely in adults, including stroke, visual loss, and death. A myocardial infarction has been reported in a 14-year-old male following the use of oral sumatriptan; clinical signs occurred within 1 day of drug administration. Clinical data to determine the frequency of serious adverse reactions in pediatric patients who might receive subcutaneous, oral, or intranasal sumatriptan are not presently available.

8.5 Geriatric Use

Clinical trials of sumatriptan injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

A cardiovascular evaluation is recommended for geriatric patients who have other cardiovascular risk factors (e.g., diabetes, hypertension, smoking, obesity, strong family history of CAD) prior to receiving ALSUMA [see *Warnings and Precautions (5.1)*].

10 OVERDOSAGE

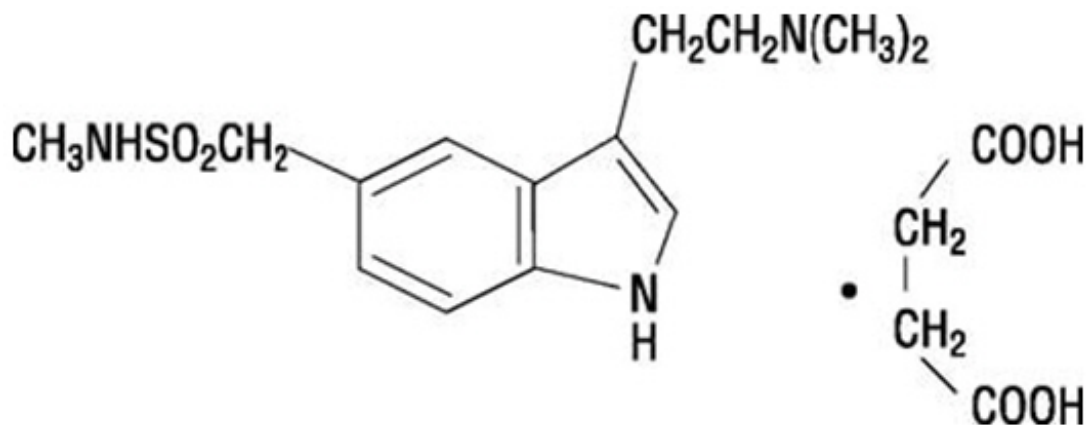
Data on overdose of Alsuma and its treatment are lacking in humans. Overdoses would be expected from animal data (dogs at 0.1 g/kg, rats at 2 g/kg) to possibly cause convulsions, tremor, inactivity, erythema of the extremities, reduced respiratory rate, cyanosis, ataxia, mydriasis, injection site reactions (desquamation, hair loss, and scab formation), and paralysis.

The elimination half-life of sumatriptan is about 2 hours [see *Clinical Pharmacology (12.3)*], and therefore monitoring of patients after overdose with subcutaneous sumatriptan should continue for at least 10 hours or while symptoms or signs persist.

It is unknown what effect hemodialysis or peritoneal dialysis has on the serum concentrations of sumatriptan.

11 DESCRIPTION

ALSUMA contains sumatriptan succinate, a selective 5-HT_{1B/1D} receptor agonist. Sumatriptan succinate is chemically designated as 3-[2-(dimethylamino)ethyl]-N-methyl-indole-5-methanesulfonamide succinate (1:1), and it has the following structure:



The empirical formula is $C_{14}H_{21}N_3O_2S \cdot C_4H_6O_4$, representing a molecular weight of 413.5. Sumatriptan succinate is a white to off-white powder that is readily soluble in water and in saline.

ALSUMA is a clear, colorless to pale yellow, sterile, nonpyrogenic solution for subcutaneous injection. Each 0.5 mL of ALSUMA 12 mg/mL solution contains 6 mg of sumatriptan (base) as the succinate salt and 3.5 mg of sodium chloride, USP in Water for Injection, USP. The pH range of the solution is approximately 4.2 to 5.3.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Sumatriptan binds with high affinity to human cloned 5-HT_{1B/1D} receptors. Sumatriptan presumably exerts its therapeutic effects in the treatment of migraine headache through agonist effects at the 5-HT_{1B/1D} receptors on intracranial blood vessels and sensory nerves of the trigeminal system, which result in cranial vessel constriction and inhibition of pro-inflammatory neuropeptide release.

12.2 Pharmacodynamics

Blood Pressure:

Significant elevation in blood pressure, including hypertensive crisis, has been reported in patients with and without a history of hypertension [see *Warnings and Precautions (5.8)*].

Peripheral (Small) Arteries:

In healthy volunteers (N = 18), a trial evaluating the effects of sumatriptan on peripheral (small vessel) arterial reactivity failed to detect a clinically significant increase in peripheral resistance.

Heart Rate:

Transient increases in blood pressure observed in some subjects in clinical trials carried out during sumatriptan's development as a treatment for migraine were not accompanied by any clinically significant changes in heart rate.

12.3 Pharmacokinetics

Absorption and Bioavailability:

The bioavailability of sumatriptan via subcutaneous site injection to 18 healthy male subjects was 97% ± 16% of that obtained following intravenous injection.

After a single 6-mg subcutaneous manual injection into the deltoid area of the arm in 18 healthy males (age: 24 ± 6 years, weight: 70 kg), the maximum serum concentration (C_{max}) of sumatriptan was (mean ± standard deviation) 74 ± 15 ng/mL and the time to peak concentration (T_{max}) was 12 minutes after injection (range: 5 to 20 minutes). In this trial, the same dose injected subcutaneously in the thigh gave a

C_{\max} of 61 ± 15 ng/mL by manual injection versus 52 ± 15 ng/mL by autoinjector techniques. The T_{\max} or amount absorbed was not significantly altered by either the site or technique of injection.

Distribution:

Protein binding, determined by equilibrium dialysis over the concentration range of 10 to 1,000 ng/mL, is low, approximately 14% to 21%. The effect of sumatriptan on the protein binding of other drugs has not been evaluated.

Following a 6-mg subcutaneous injection into the deltoid area of the arm in 9 males (mean age: 33 years, mean weight: 77 kg) the volume of distribution central compartment of sumatriptan was 50 ± 8 liters and the distribution half-life was 15 ± 2 minutes.

Metabolism:

In vitro studies with human microsomes suggest that sumatriptan is metabolized by MAO, predominantly the A isoenzyme. Most of a radiolabeled dose of sumatriptan excreted in the urine is the major metabolite indole acetic acid (IAA) or the IAA glucuronide, both of which are inactive.

Elimination:

After a single 6-mg subcutaneous dose, $22\% \pm 4\%$ was excreted in the urine as unchanged sumatriptan and $38\% \pm 7\%$ as the IAA metabolite.

Following a 6-mg subcutaneous injection into the deltoid area of the arm, the systemic clearance of sumatriptan was $1,194 \pm 149$ mL/min and the terminal half-life was 115 ± 19 minutes.

Special Populations:

Age: The pharmacokinetics of sumatriptan in the elderly (mean age: 72 years, 2 males and 4 females) and in subjects with migraine (mean age: 38 years, 25 males and 155 females) were similar to that in healthy male subjects (mean age: 30 years).

Renal Impairment: The effect of renal impairment on the pharmacokinetics of sumatriptan has not been examined.

Hepatic Impairment: The effect of mild to moderate hepatic disease on the pharmacokinetics of subcutaneously administered sumatriptan has been evaluated. There were no significant differences in the pharmacokinetics of subcutaneously administered sumatriptan in moderately hepatically impaired subjects compared with healthy controls. The pharmacokinetics of subcutaneously administered sumatriptan in patients with severe hepatic impairment has not been studied. The use of ALSUMA in this population is contraindicated [see *Contraindications (4)*].

Race: The systemic clearance and C_{\max} of sumatriptan were similar in black ($n = 34$) and Caucasian ($n = 38$) healthy male subjects.

Drug Interaction Studies:

Monoamine Oxidase-A Inhibitors:

In a trial of 14 healthy females, pretreatment with an MAO-A inhibitor decreased the clearance of sumatriptan, resulting in a 2-fold increase in the area under the sumatriptan plasma concentration-time curve (AUC), corresponding to a 40% increase in elimination half-life.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis: In carcinogenicity studies in mouse and rat, sumatriptan was administered orally for 78 and 104 weeks, respectively, at doses up to 160 mg/kg/day (the high dose in rat was reduced from 360 mg/kg/day during week 21). There was no evidence in either species of an increase in tumors related to sumatriptan administration.

Mutagenesis: Sumatriptan was negative in in vitro (bacterial reverse mutation [Ames], gene cell mutation in Chinese hamster V79/HGPRT, chromosomal aberration in human lymphocytes) assay and in vivo (rat micronucleus) assays.

Impairment of Fertility: When sumatriptan (5, 50, 500 mg/kg/day) was administered orally to male and female rats prior to and throughout the mating period, there was a treatment-related decrease in fertility secondary to a decrease in mating in animals treated with doses greater than 5 mg/kg/day. It is not clear whether this finding was due to an effect on males or females or both.

13.2 Animal Toxicology and/or Pharmacology

Corneal Opacities:

Dogs receiving oral sumatriptan developed corneal opacities and defects in the corneal epithelium. Corneal opacities were seen at the lowest dosage tested, 2 mg/kg/day, and were present after 1 month of treatment. Defects in the corneal epithelium were noted in a 60-week study. Earlier examinations for these toxicities were not conducted and no-effect doses were not established.

14 CLINICAL STUDIES

14.1 Migraine

In controlled clinical trials enrolling more than 1,000 subjects during migraine attacks who were experiencing moderate or severe pain and 1 or more of the symptoms enumerated in Table 3, onset of relief began as early as 10 minutes following a 6-mg sumatriptan injection. Lower doses of sumatriptan injection may also prove effective, although the proportion of subjects obtaining adequate relief was decreased and the latency to that relief is greater with lower doses.

In Study 1, 6 different doses of sumatriptan injection (n = 30 each group) were compared with placebo (n = 62), in a single-attack, parallel-group design, the dose response relationship was found to be as shown in Table 2.

Table 2. Proportion of Subjects With Migraine Relief and Incidence of Adverse Events by Time and by Sumatriptan Dose in Study 1

| Dose of Sumatriptan Injection | Percent Subjects with Relief* | | | | Adverse Events Incidence (%) |
|-------------------------------|-------------------------------|---------------|-----------|------------|------------------------------|
| | at 10 Minutes | at 30 Minutes | at 1 Hour | at 2 Hours | |
| Placebo | 5 | 15 | 24 | 21 | 55 |
| 1 mg | 10 | 40 | 43 | 40 | 63 |
| 2 mg | 7 | 23 | 57 | 43 | 63 |
| 3 mg | 17 | 47 | 57 | 60 | 77 |
| 4 mg | 13 | 37 | 50 | 57 | 80 |
| 6 mg | 10 | 63 | 73 | 70 | 83 |
| 8 mg | 23 | 57 | 80 | 83 | 93 |

* Relief is defined as the reduction of moderate or severe pain to no pain or mild pain after dosing without use of rescue medication.

In 2 randomized, placebo-controlled clinical trials of sumatriptan injection 6 mg in 1,104 subjects with moderate or severe migraine pain (Studies 2 and 3), the onset of relief was less than 10 minutes. Headache relief, as defined by a reduction in pain from severe or moderately severe to mild or no headache, was achieved in 70% of the subjects within 1 hour of a single 6-mg subcutaneous dose of sumatriptan injection. Approximately 82% and 65% of subjects treated with sumatriptan 6 mg had headache relief and were pain free within 2 hours, respectively.

Table 3 shows the 1- and 2-hour efficacy results for sumatriptan injection 6 mg in Studies 2 and 3.

Table 3. Proportion of Subjects With Pain Relief and Relief of Migraine Symptoms After 1 and 2 Hours of Treatment in Studies 2 and 3

| 1-Hour Data | Study 2 | | Study 3 | |
|---|--------------------|--|--------------------|--|
| | Placebo (n=190) | Sumatriptan Succinate 6 mg (n=384) | Placebo (n=180) | Sumatriptan Succinate 6 mg (n=350) |
| Subjects with pain relief (grade 0/1) | 18% | 70%* | 26% | 70%* |
| Subjects with no pain | 5% | 48%* | 13% | 49%* |
| Subjects without nausea | 48% | 73%* | 50% | 73%* |
| Subjects without photophobia | 23% | 56%* | 25% | 58%* |
| Subjects with little or no clinical disability [†] | 34% | 76%* | 34% | 76%* |

| 2-Hour Data | Study 2 | | Study 3 | |
|---|----------------------|---|----------------------|---|
| | Placebo [‡] | Sumatriptan Succinate 6 mg [§] | Placebo [‡] | Sumatriptan Succinate 6 mg [§] |
| Subjects with pain relief (grade 0/1) | 31% | 81%* | 39% | 82%* |
| Subjects with no pain | 11% | 63%* | 19% | 65%* |
| Subjects without nausea | 56% | 82%* | 63% | 81%* |
| Subjects without photophobia | 31% | 72%* | 35% | 71%* |
| Subjects with little or no clinical disability [†] | 42% | 85%* | 49% | 84%* |

* $P < 0.05$ versus placebo.

[†] A successful outcome in terms of clinical disability was defined prospectively as ability to work mildly impaired or ability to work and function normally.

[‡] Includes subjects that may have received an additional placebo injection 1 hour after the initial injection.

[§] Includes subjects that may have received an additional 6 mg of sumatriptan injection 1 hour after the initial injection.

Sumatriptan injection also relieved photophobia, phonophobia (sound sensitivity), nausea, and vomiting associated with migraine attacks.

The efficacy of sumatriptan injection was unaffected by whether or not the migraine was associated with aura, duration of attack, gender or age of the subject, or concomitant use of common migraine prophylactic drugs (e.g., beta-blockers).

14.2 Cluster Headache

The efficacy of sumatriptan injection in the acute treatment of cluster headache was demonstrated in 2 randomized, double-blind, placebo-controlled, 2-period crossover trials (Studies 4 and 5). Subjects aged 21 to 65 years were enrolled and were instructed to treat a moderate to very severe headache within 10 minutes of onset. Headache relief was defined as a reduction in headache severity to mild or no pain. In both trials, the proportion of individuals gaining relief at 10 or 15 minutes was significantly

greater among subjects receiving 6 mg of sumatriptan injection compared with those who received placebo (see Table 4).

Table 4. Proportion of Subjects With Cluster Headache Relief by Time in Studies 4 and 5

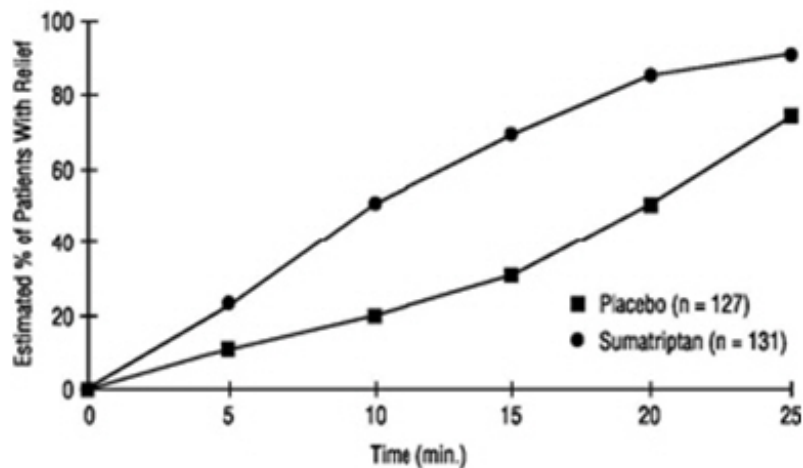
| | Study 4 | | Study 5 | |
|-------------------------------------|-------------------|--|-------------------|--|
| | Placebo (n=39) | Sumatriptan Succinate 6 mg (n=39) | Placebo (n=88) | Sumatriptan Succinate 6 mg (n=92) |
| Subjects with Pain Relief (no/mild) | | | | |
| 5 Minutes post-injection | 8% | 21% | 7% | 23% ^a |
| 10 Minutes post-injection | 10% | 49% ^a | 25% | 49% ^a |
| 15 Minutes post-injection | 26% | 74% ^a | 35% | 75% ^a |

^aP<0.05.

(n = Number of headaches treated).

An estimate of the cumulative probability of a subject with a cluster headache obtaining relief after being treated with either sumatriptan injection or placebo is presented in Figure 1.

Figure 1. Time to Relief of Cluster Headache from Time of Injection*



* The figure uses Kaplan-Meier (product limit) Survivorship Plot. Subjects taking rescue medication were censored at 15 minutes.

The plot was constructed with data from subjects who either experienced relief or did not require (request) rescue medication within a period of 2 hours following treatment. As a consequence, the data in the plot are derived from only a subset of the 258 headaches treated (rescue medication was required in 52 of the 127 placebo-treated headaches and 18 of the 131 headaches treated with sumatriptan injection).

Other data suggest that treatment with sumatriptan injection is not associated with an increase in early recurrence of headache and has little effect on the incidence of later-occurring headaches (i.e., those occurring after 2, but before 18 or 24 hours).

16 HOW SUPPLIED/STORAGE AND HANDLING

ALSUMA contains sumatriptan (base) as the succinate salt and is supplied as a clear, colorless to pale yellow, sterile, nonpyrogenic solution in a single-dose pre-filled auto-injector.

| Injection Strength | Package Contents | NDC# |
|---------------------------|--|--------------|
| 6 mg | Two 6 mg single dose ALSUMA (sumatriptan injection) 6 mg/0.5 mL Auto-Injectors ALSUMA Physician Insert Patient Instructions for Use | 0069-0138-02 |

Store at 25°C, excursions permitted 15° to 30°C (59° to 86° F). Protect from light. Do not refrigerate.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for Use).

Risk of Myocardial Ischemia and/or Infarction, Prinzmetal's Angina, Other Vasospasm-Related Events, Arrhythmias, and Cerebrovascular Events

Inform patients that ALSUMA may cause serious cardiovascular side effects such as myocardial infarction or stroke. Although serious cardiovascular events can occur without warning symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath, irregular heartbeat, significant rise in blood pressure, weakness, and slurring of speech and should ask for medical advice when observing any indicative sign or symptoms. Patients should be apprised of the importance of this follow-up [see *Warnings and Precautions* (5.1, 5.2, 5.4, 5.5, 5.8)].

Anaphylactic/Anaphylactoid Reactions

Inform patients that anaphylactic/anaphylactoid reactions have occurred in patients receiving sumatriptan injection. Such reactions can be life threatening or fatal. In general, anaphylactic reactions to drugs are more likely to occur in individuals with a history of sensitivity to multiple allergens [see *Contraindications* (4) and *Warnings and Precautions* (5.9)].

Serotonin Syndrome

Patients should be cautioned about the risk of serotonin syndrome with the use of ALSUMA or other triptans, particularly during combined use with SSRIs, SNRIs, TCAs, and MAO inhibitors [see *Warnings and Precautions* (5.7) and *Drug Interactions* (7.4)].

Medication Overuse Headache

Inform patients that use of acute migraine drugs for 10 or more days per month may lead to an exacerbation of headache and encourage patients to record headache frequency and drug use (e.g., by keeping a headache diary) [see *Warnings and Precautions* (5.6)].

Pregnancy

Inform patients that ALSUMA should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus [see *Use in Specific Populations* (8.1)].

Nursing Mothers

Advise patients to notify their healthcare provider if they are breastfeeding or plan to breastfeed [see *Use in Specific Populations* (8.3)].

Ability to Perform Complex Tasks

Since migraines or treatment with ALSUMA may cause somnolence and dizziness, instruct patients to evaluate their ability to perform complex tasks during migraine attacks and after administration of ALSUMA.

How to Use ALSUMA

ALSUMA is a pre-filled, fully-assembled, single-use device intended to deliver a 6 mg dose of sumatriptan.

Provide patients instruction on the proper use of ALSUMA if they are able to self-administer ALSUMA in a medically unsupervised situation.

Inform patients that the injection is only intended to be given subcutaneously. Intramuscular or intravascular delivery should be avoided. Instruct patients to use injection sites with an adequate skin and subcutaneous thickness to accommodate the length of the needle (e.g. lateral thigh or upper arms).

Manufactured by :

Meridian Medical Technologies, Inc., Columbia, MD 21046

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Division of Pfizer Inc.

NY, NY 10017

LAB-0650-2.0

Patient Information

ALSUMA™ (Awl-SOO'-mah)

(sumatriptan injection)

Auto-Injector

Read this Patient Information before you start taking ALSUMA and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about ALSUMA?

ALSUMA can cause serious side effects, including:

Heart attack and other heart problems. Heart problems may lead to death.

Stop taking ALSUMA and get emergency medical help right away if you have any of the following symptoms of a heart attack:

- discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw, or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

ALSUMA is not for people with risk factors for heart disease unless a heart exam is done and shows no problem. You have a higher risk for heart disease if you:

- have high blood pressure
- have high cholesterol levels

- smoke
- are overweight
- have diabetes
- have a family history of heart disease

What is ALSUMA?

ALSUMA Auto-Injector is a prescription medicine used to treat acute migraine headaches with or without aura and acute cluster headaches in adults who have been diagnosed with migraine or cluster headaches.

ALSUMA is not used to treat other types of headaches such as hemiplegic (that make you unable to move on one side of your body) or basilar (rare form of migraine with aura) migraines.

ALSUMA is not used to prevent or decrease the number of migraine or cluster headaches you have. It is not known if ALSUMA is safe and effective in children under 18 years of age.

Who should not take ALSUMA?

Do not take ALSUMA if you have:

- heart problems or a history of heart problems
- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)
- uncontrolled high blood pressure
- hemiplegic migraines or basilar migraines. If you are not sure if you have these types of migraines, ask your healthcare provider.
- had a stroke, transient ischemic attacks (TIAs), or problems with your blood circulation
- taken any of the following medicines in the last 24 hours:
 - almotriptan (AXERT[®])
 - eletriptan (RELPA[®])
 - frovatriptan (FROVA[®])
 - naratriptan (AMERGE[®])
 - rizatriptan (MAXALT[®], MAXALT-MLT[®])
 - sumatriptan (IMITREX[®])
 - sumatriptan and naproxen (TREXIMET[®])
 - ergotamines (CAFERGOT[®], ERGOMAR[®], MIGERGOT[®])
 - dihydroergotamine (D.H.E. 45[®], MIGRANAL[®])

Ask your healthcare provider if you are not sure if your medicine is listed above.

- an allergy to sumatriptan or any of the ingredients in ALSUMA. See the end of this leaflet for a complete list of ingredients in ALSUMA.

What should I tell my healthcare provider before taking ALSUMA?

Before you take ALSUMA, tell your healthcare provider about all of your medical conditions, including if you:

- have high blood pressure
- have high cholesterol
- have diabetes
- smoke
- are overweight
- have heart problems or family history of heart problems or stroke
- have liver problems
- have had epilepsy or seizures
- are not using effective birth control
- become pregnant while taking ALSUMA

- are breastfeeding or plan to breastfeed. ALSUMA passes into your breast milk and may harm your baby. Talk with your healthcare provider about the best way to feed your baby if you take ALSUMA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Using ALSUMA with certain other medicines can affect each other, causing serious side effects.

Especially tell your healthcare provider if you take anti-depressant medicines called:

- selective serotonin reuptake inhibitors (SSRIs)
- serotonin norepinephrine reuptake inhibitors (SNRIs)
- tricyclic antidepressants (TCAs)
- monoamine oxidase inhibitors (MAOIs)

Ask your healthcare provider or pharmacist for a list of these medicines if you are not sure.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take ALSUMA?

- **Read the Instructions for Use that come with ALSUMA.**
- Certain people should take their first dose of ALSUMA in their healthcare provider's office or in another medical setting. Ask your healthcare provider if you should take your first dose in a medical setting.
- Use ALSUMA exactly as your healthcare provider tells you to use it.
- Your healthcare provider may change your dose. Do not change your dose without first talking with your healthcare provider.
- Do not give ALSUMA into a vein.
- Give the injection in the side of your thigh, or the upper arm just below the skin (subcutaneous). Check with your healthcare provider if you are not sure where to inject yourself.
- You should give an injection as soon as the symptoms of your headache start, but it may be given at any time during a migraine attack.
- If you did not get any relief after the first injection, do not give a second injection without first talking with your healthcare provider.
- You can take a second injection 1 hour after the first injection, but not sooner, if your headache came back after your first injection.
- Do not take more than 2 doses of ALSUMA in 24 hours.
- If you use too much ALSUMA, call your healthcare provider or go to the nearest hospital emergency room right away.
- You should write down when you have headaches and when you take ALSUMA so you can talk with your healthcare provider about how ALSUMA is working for you.

What should I avoid while taking ALSUMA?

ALSUMA can cause dizziness, weakness, or drowsiness. If you have these symptoms, do not drive a car, use machinery, or do anything where you need to be alert.

What are the possible side effects of ALSUMA?

ALSUMA can cause serious side effects. See "What is the most important information I should know about ALSUMA?"

These serious side effects include:

- stroke
- changes in color or sensation in your fingers and toes (Raynaud's syndrome)
- **stomach and intestinal problems (gastrointestinal and colonic ischemic events).**

Symptoms of gastrointestinal and colonic ischemic events include:

- sudden or severe stomach pain
- stomach pain after meals
- weight loss
- nausea or vomiting
- constipation or diarrhea
- bloody diarrhea
- fever
- **problems with blood circulation to your legs and feet (peripheral vascular ischemia).**

Symptoms of peripheral vascular ischemia include:

- cramping and pain in your legs or hips
- feeling of heaviness or tightness in your leg muscles
- burning or aching pain in your feet or toes while resting
- numbness, tingling, or weakness in your legs
- cold feeling or color changes in 1 or both legs or feet
- **medication overuse headaches.** Some people who use too many ALSUMA injections may have worse headaches (medication overuse headache). If your headaches get worse, your healthcare provider may decide to stop your treatment with ALSUMA.
- **serotonin syndrome.** Serotonin syndrome is a rare but serious problem that can happen in people using ALSUMA, especially if ALSUMA is used with anti-depressant medicines called SSRIs or SNRIs.

Call your healthcare provider right away if you have any of the following symptoms of serotonin syndrome:

- mental changes such as seeing things that are not there (hallucinations), agitation, or coma
- fast heartbeat
- changes in blood pressure
- high body temperature
- tight muscles
- trouble walking
- **seizures.** Seizures have happened in people taking ALSUMA who have never had seizures before. Talk with your healthcare provider about your chance of having seizures while you take ALSUMA.

The most common side effects of ALSUMA include:

- bleeding, swelling, redness, bruising and pain at the injection site
- tingling or numbness in your fingers or toes
- dizziness
- warm, hot, burning feeling to your face (flushing)
- discomfort or stiffness in your neck
- feeling weak, drowsy, or tired

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of ALSUMA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ALSUMA?

Store ALSUMA between 59°F to 86°F (15°C to 30°C).

- Store your medicine away from light.
- Do not put ALSUMA in the refrigerator.

- Keep each ALSUMA Auto-Injector in its storage and disposal case.
- Remove the ALSUMA Auto-Injector from the storage and disposal case only when you need to give yourself an injection.

Keep ALSUMA and all medicines out of the reach of children.

General information about the safe and effective use of ALSUMA

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use ALSUMA for a condition for which it was not prescribed. Do not give ALSUMA to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about ALSUMA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ALSUMA that is written for healthcare professionals.

For more information, go to www.alsuma.com or call 1-877-770-8796.

What are the ingredients in ALSUMA?

Active ingredient: sumatriptan succinate
 Inactive ingredients: sodium chloride, water for injection

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

4/14

LAB-0651-2.0

PATIENT INSTRUCTIONS FOR USE

**ALSUMA™ (Awl-SOO'-mah)
 (sumatriptan injection)
 Auto-Injector**

Read the Patient Instructions for Use that come with the ALSUMA™ Auto-Injector before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your healthcare provider about your medical condition or your treatment.

Before you use ALSUMA for the first time, make sure your healthcare provider teaches you the right way to use it.

Follow these instructions each time you use ALSUMA.

ALSUMA is a disposable one time use, prefilled auto-injector used for the treatment of acute migraine or cluster headaches.

Each ALSUMA Auto-Injector is filled with medicine and ready to use. No assembly is required.

ALSUMA is packaged with two doses to a box, with each ALSUMA dose stored in a separate storage and disposal case. (see Figure 1)



[Figure 1]

ALSUMA Important Tips

- Do not remove the Blue Safety Release until you are ready to inject yourself.
- Do not place your fingers on the top or the bottom end of the ALSUMA Auto-Injector.
- Do not touch the orange needle end.
- Always point the orange needle end down.
- Do not take apart the ALSUMA Auto-Injector.
- **Keep out of the reach of children.**

The Storage and Disposal Case (see Figure 2)



[Figure 2]

- Always store and carry ALSUMA in the storage and disposal case.
- Do not remove ALSUMA from the storage and disposal case until you are ready to use it.
- **Always keep the orange needle end facing the bottom of the storage and disposal case.**
- The purple cap should be screwed tightly onto the storage and disposal case before use.
- After your injection, the ALSUMA Auto-Injector should be placed back into the storage and disposal case. Throw away the case the way your healthcare provider told you.

The ALSUMA Auto-Injector

[Figure 3]



- When the Blue Safety Release is in place, ALSUMA is locked and will not inject. (see Figure 3)

[Figure 4]



- When the Blue Safety Release is taken off, ALSUMA is unlocked and ready to use. (see Figure 4)

Holding the ALSUMA Auto-Injector

Always hold the ALSUMA Auto-Injector in the middle with the orange **needle end** pointing down. (see Figure 5)

- **Never** hold the injector upside down. (see Figure 6)
- **Never** put your thumb on either end of the injector. (see Figures 7 and 8)
- **Never** touch the orange **needle end**. (see Figure 8)



[Figure 5]

[Figure 6]

[Figure 7]

[Figure 8]

How to Use ALSUMA

1. Choose an injection site.

- Ask your doctor about where you should inject yourself (usually the side of your thigh or your upper arm). (see Figures 9 and 10)
- Do not inject through your clothes.



[Figure 9]

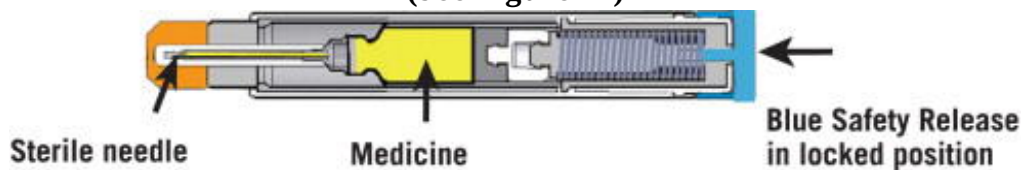


[Figure 10]

2. Preparing your ALSUMA Auto-Injector.

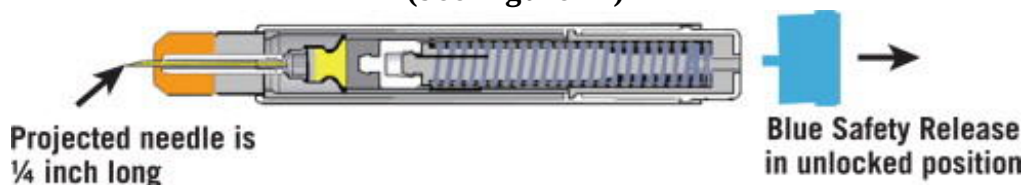
An Inside Look

ALSUMA (SUMATRIPTAN INJECTION) 6 mg/0.5 mL AUTO-INJECTOR BEFORE ACTIVATION
(see Figure 11)



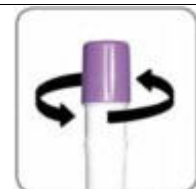
[Figure 11]

ALSUMA (SUMATRIPTAN INJECTION) 6 mg/0.5 mL AUTO-INJECTOR WHEN ACTIVATED
(see Figure 12)



[Figure 12]

- Twist off the purple cap from the storage and disposal case. (see Figure 13)



[Figure 13]

- Slide the ALSUMA Auto-Injector out into your hand. (see Figure 14)



[Figure 14]

- Hold the ALSUMA Auto-Injector in the middle. (see Figure 15)



[Figure 15]

- Pull off the Blue Safety Release to unlock the ALSUMA Auto-Injector. (see Figure 16)



[Figure 16]

3. Giving your injection.

Give yourself the injection exactly the way your healthcare provider showed you.

- Place the orange needle end on your skin where you will give the injection. (see Figures 17 and 18)



[Figure 17]

- Push the ALSUMA Auto-Injector hard into your skin until you feel a jolt. (see Figures 17 and 18)



[Figure 18]

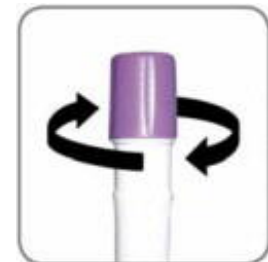
- Hold the ALSUMA Auto-Injector in place for 5 seconds to deliver the medicine. (see Figures 17 and 18)

4. After your injection, throw away (dispose of) the ALSUMA Auto-Injector.

- Place the uncapped, empty storage and disposal case onto a flat surface. (see Figure 19)
- Slowly insert the orange needle end of the used injector into the open end of the storage and disposal case. Slide the entire used injector into the case. (see Figure 19)
- Tilt up the open end of the storage and disposal case and screw on the purple cap. (see Figure 20)



[Figure 19]



[Figure 20]

Check with your healthcare provider about the right way to throw away your used ALSUMA Auto-Injector. Each ALSUMA Auto-Injector can be used only **one** time.

Important Tips on Storing and Using Your Auto-Injector

- Store the ALSUMA Auto-Injector between 59°F to 86°F (15°C–30°C).
- Keep the ALSUMA Auto-Injector out of the light.
- Do not put the ALSUMA Auto-Injector in the refrigerator.
- Keep each ALSUMA Auto-Injector in its storage and disposal case.
- Remove the ALSUMA Auto-Injector from the storage and disposal case only when you need to give yourself an injection.

ALSUMA is a trademark of Meridian Medical Technologies[®], Inc.

04/2014

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NY, NY 10017

LAB-0652-2.0

Principal Display Panel - Syringe, Glass Label

See other side for instructions

Rx only

For subcutaneous
injection only.

Each 0.5 mL
injection
contains 6mg
sumatriptan
(as the succinate
salt) and 3.5 mg
of sodium
chloride

ALSUMA
(*sumatriptan injection*)

6mg/0.5mL
Auto-Injector

STORE AT 25°C (77°F); EXCURSIONS
PERMITTED TO 15-30°C (59-86°F)
DO NOT REFRIGERATE
PROTECT FROM LIGHT

Distributed by:

Pfizer Labs, Division of Pfizer Inc.
NY, NY 10017

VIEWING WINDOW

APPEARS RED IF UNIT USED

Manufactured by:
Meridan Medical Technologies, Inc.
Columbia, MD 21046
a Pfizer Inc. company

ALSUMA TM
(sumatriptan injection)
6mg/0.5mL
Auto-Injector

See other side for instructions

Rx only

For subcutaneous injection only.

Each 0.5 mL injection contains 6 mg sumatriptan (as the succinate salt) and 3.5 mg of sodium chloride



STEP 1

GRASP then **PULL OFF** **Blue Safety Release** to unlock.



NEEDLE END

STEP 2

PLACE orange **NEEDLE END** against the injection site. **PUSH HARD** until it jolts.



STEP 3

Now **HOLD IN PLACE** for **5 seconds**.

ALSUMA TM
(sumatriptan injection)
6mg/0.5mL
Auto-Injector

STORE AT 25°C (77°F); EXCURSIONS PERMITTED TO 15-30°C (59-86°F)
DO NOT REFRIGERATE
PROTECT FROM LIGHT

Distributed by:
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NY, NY 10017

VIEWING WINDOW

APPEARS RED IF UNIT USED

Manufactured by:
Meridian Medical Technologies, Inc.
Columbia, MD 21046
a Pfizer Inc. company

0001684

NEEDLE END **NEEDLE END** **NEEDLE END**



Principal Display Panel – Carton Label

NDC 0069-0138-02

ALSUMA™

(sumatriptan injection)

6mg/0.5mL

Auto-Injector

**For subcutaneous
injection only.**

ALSUMA 
 (sumatriptan injection)
 6mg/0.5mL
 Auto-Injector

For subcutaneous injection only.

Rx only

NDC 0069-0138-02



2 pre-assembled ALSUMA (sumatriptan injection) Auto-Injectors ready for use

0001685



NDC 0069-0138-02

Rx only

ALSUMA 
 (sumatriptan injection)
 6mg/0.5mL
 Auto-Injector

This carton contains:
 - 2 pre-assembled 0.5 mL auto-injectors, each containing 6 mg of sumatriptan (as the succinate salt) for subcutaneous injection only
 - 2 storage/disposal cases
 - Instructions for Use
 - Prescribing Information

ALSUMA 
 (sumatriptan injection)
 6mg/0.5mL
 Auto-Injector

See package insert for Dosage and Administration.

For subcutaneous injection only.



ALSUMA 
 (sumatriptan injection)
 6mg/0.5mL
 Auto-Injector

Each auto-injector contains 0.5 mL of solution containing 6 mg of sumatriptan (as the succinate salt) and 3.5 mg of sodium chloride. For subcutaneous injection only. See full Prescribing Information for Dosage and Administration. Store at 25°C (77°F). Excursions permitted to 15°-30°C (59°-86° F). Do not refrigerate. Protect from light.

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Keep Out Of Reach Of Children Before And After Use.

For medical advice about adverse reactions, contact your medical professional. To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

| | | |
|---|--|---|
| <p>3 GIVE THE INJECTION</p>  <p>Push hard until it jolts. Hold the auto-injector in place for 5 seconds to deliver the drug.</p>  <p>Place the orange needle end against the injection site (either bare thigh or bare upper arm).</p> | <p>2 PREPARING THE AUTO-INJECTOR</p>  <p>Pull off the blue safety release to unlock the auto-injector.</p>  <p>Grasp the auto-injector in the center.</p> | <p>1 REMOVING THE AUTO-INJECTOR FROM THE STORAGE/DISPOSAL CASE</p>  <p>Slide ALSUMA (sumatriptan injection) auto-injector out into your hand.</p>  <p>Twist off the purple cap on the storage/disposal case.</p> |
|---|--|---|

NDC 0069-0138-02

INSTRUCTIONS FOR GIVING INJECTION

ALSUMA 
 (sumatriptan injection)
 6mg/0.5mL
 Auto-Injector

OPEN THIS END



ALSUMA

sumatriptan injection, solution

Product Information

| | | | |
|--------------------------------|-------------------------------|---------------------------|---------------|
| Product Type | HUMAN PRESCRIPTION DRUG LABEL | Item Code (Source) | NDC:0069-0138 |
| Route of Administration | SUBCUTANEOUS | DEA Schedule | |

Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|---------------------------|--------------------------|-----------------|
| SUMATRIPTAN (SUMATRIPTAN) | SUMATRIPTAN | 6 mg in 0.5 mL |

Inactive Ingredients

| Ingredient Name | Strength |
|------------------------|-----------------|
| SODIUM CHLORIDE | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|----------|------------------|-----------------------------|-----------------------------|---------------------------|
| 1 | NDC:0069-0138-02 | 2 in 1 CARTON | | |
| 1 | NDC:0069-0138-01 | 0.55 mL in 1 SYRINGE, GLASS | | |

Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|---------------------------|---|-----------------------------|---------------------------|
| NDA | NDA022041 | 08/31/2009 | |

Labeler - Pfizer Laboratories Div Pfizer Inc (134489525)

Establishment

| Name | Address | ID/FEI | Business Operations |
|---|----------------|---------------|----------------------------|
| Meridian Medical Technologies, a Pfizer Company | | 167671341 | MANUFACTURE(0069-0138) |

Revised: 5/2014

Pfizer Laboratories Div Pfizer Inc